85. The method according to claim 83 wherein said triple stranded complex is at least six bases in length and each of the two different nucleic acid A binding probes C individually contribute at least one but less than eleven bases to said triple stranded complex.--

Cont.

## REMARKS

Reconsideration and withdrawal of the rejections made in the September 27, 1999 Office Action is respectfully requested in view of the above amendments and the following comments.

The specification was objected to regarding the Brief Description of the Drawings. The description has been amended as suggested by the Examiner. In view of these amendments applicant requests that this objection be withdrawn.

Claims 2, 4, 26 and 27 were rejected under 35 USC §112, first paragraph, as lacking enablement. Claims 1-30 have been canceled and new claims added to the application which more clearly define the present invention. In view of the cancellation of claims 1-30 and the addition of new claims to the application, applicant requests that this rejection be withdrawn.

Claims 1-21, 23-24 and 26-30 were rejected under 35 USC §112, second paragraph, as indefinite. Claims 1-30 have been canceled and new claims added to the application which are believed to overcome the indefiniteness issues. In

addition, applicants point out figures 3 and 4 which show more than one molecule C (i.e. molecules with different sequences which bind to different parts of nucleic acid A). As shown in figures 3 and 4, all molecules of C which participate in the triple stranded complex bind to molecule A at the same time. In other words, "strand C" of the triple stranded complex may be composed of an aggregate of molecules C. The new claim language is believed to clarify this issue. Support for the language that molecules B and C are probes and that the binding region of probe C is longer than the binding region of probe B can be found at page 14, first and third full paragraphs, of the present application. In view of the cancellation of claims 1-30 and the addition of new claims to the application, applicants request that this rejection be withdrawn.

Claims 1-6, 9-14, 16-19 and 21-27 were rejected under 35 USC §103 as unpatentable over T'so in view of Vardimon. Applicants respectfully contend that Vardimon is not properly combined with the other cited references. Vardimon relates to a pharmaceutical composition and method for treating injury to or diseases which result in neurological degeneration resulting from stroke, brain, retina or spinal cord injuries (See: Abstract). The passage at col. 13, lines 41-59, which is cited in the Office Action, refers to an experimental procedure directed to the quantitation of bulk nucleic acid which has been obtained and then separated into fragments using electrophoresis. Detection of DNA fragments from lysed tissue cells is performed using an intercalating dye which does not discriminate with respect to the nucleic acid. The present claims are directed to the detection

of a particular nucleic acid molecule A by the specific formation of a triple stranded binding complex followed by specific detection and quantitation of said triple stranded complex. Because the use of an intercalation dye in the present invention would not provide specific detection of the triple stranded complex, the method of Vardimon is so fundamentally different it is not properly combined with any of the cited art to achieve specific detection or quantitation of the triple stranded complex.

Ts'o is primarily directed to the introduction of new nucleosides which facilitate triplex formation using new binding motifs not possible using only naturally occurring nucleosides (See col. 3, line 9, to col. 4, line 14). Ts'o does not teach that the second and third strands comprise binding sites (sites of hybridization with the nucleic acid) of different lengths and consequently, Ts'o does not teach that either of two identical second strands or two identical third strands (wherein the second strand is different from the third strand) will form a triplex of inferior thermal stability as compared with a triplex formed using one second strand and one third strand. In addition, Ts'o does not describe or suggest a four element triplex nor describe mismatch discrimination outside the triplex stranded region. Since the independent claims in the present application all require that the aggregate binding region of the one or more probes C be longer than the binding region of probe B, the combination of Vardimon and Ts'o does not disclose all the elements of the present claims. In fact, none of the references cited by the Examiner, alone or in

combination, disclose the use of two different probes of different base sequence with each probe having a binding region (which interact with a target nucleic acid) wherein one binding region is longer than the other. In view of the fact that T'so and Vardimon do not disclose the claimed invention individually or in combination, applicants request that this rejection be withdrawn.

Claim 15 was rejected under 35 USC §103(a) as unpatentable over T'so in view of Vardimon further in view of Corey. As discussed above, T'so and Vardimon do not suggest or disclose the use of two different probes of different base sequence with each probe having a binding region which interacts with a target nucleic acid, wherein one binding region is longer than the other. Corey is cited for the disclosure of PNA as a nucleic acid analogue in nucleic acid hybridization assays and does not cure the deficiencies in T'so and Vardimon. In view of the above discussion, applicants request that this rejection be withdrawn.

Claims 28-30 were rejected under 35 USC §103(a) as unpatentable over T'so, Vardimon and Corey further in view of Buchardt. Buchardt is cited for the disclosure of general formulas of PNAs and does not cure the deficiencies in T'so, Vardimon and Corey regarding the use of two different probes of different base sequence with each probe having a binding region which interacts with a target nucleic acid, wherein one binding region is longer than the other. In view of the above discussion, applicants request that this rejection be withdrawn.

Claims 1, 3, 5, 6, 10-13, 19, 22, and 25 were rejected under 35 USC §103(a) as unpatentable over Svinarchuk in view of Vardimon. Svinarchuk is directed to compositions which form using a single probe which binds to a double stranded nucleic acid to form a triplex. The claims of the present application all require the use of two probes (B and C) to form the triple stranded complex which is then detected. Therefore, the teachings of Svinarchuk are distinctly different from the present invention. It is also noteworthy that the shortest Svinarchuk probe is longer than IO bases. Typically, the binding region of probe B of the present invention is IO or less bases in length. As discussed above, Vardimon discloses the use of an intercalation dye (i.e. ethidium bromide) which would not provide specific detection of the triple stranded complex. In view of the fact that Svinarchuk is directed only to the use of a single probe interacting with a double stranded nucleic acid target and Vardimon does not disclose a method for the specific detection or quantitation of a triple stranded complex, applicants request that this rejection be withdrawn.

Claims 1-3, 6, 13-14, 16, 19 and 25 were rejected under 35 USC §103(a) as unpatentable over Fresco in view of Vardimon. Fresco is primarily directed to the use of a single probe to form a triplex. Though Fresco is not absolutely limited to a single probe, Fresco does not suggest or disclose the use of two different probes with different base sequences, where each probe has a binding region and one probe has a binding region longer than the other. As discussed above, Vardimon

does not cure this deficiency. In view of the above discussion, applicants request that this rejection be withdrawn.

Claim 15 was rejected under 35 USC §103(a) as unpatentable over Fresco and Vardimon in view of Corey. As discussed above, Fresco and Vardimon do not suggest or disclose the use of two different probes of different base sequence with each probe having a binding region which interacts with a target nucleic acid, wherein one binding region is longer than the other. Corey is cited for the disclosure of PNA as a nucleic acid analogue in nucleic acid hybridization assays and does not cure the deficiencies in Fresco and Vardimon. In view of the above discussion, applicants request that this rejection be withdrawn.

Claims 28-30 were rejected under 35 USC §103(a) as unpatentable over Fresco, Vardimon and Corey further in view of Buchardt. Buchardt is cited for the disclosure of general formulas of PNAs and does not cure the deficiencies in Fresco, Vardimon and Corey regarding the use of two different probes of different base sequence with each probe having a binding region which interacts with a target nucleic acid, wherein one binding region is longer than the other. In view of the above discussion, applicants request that this rejection be withdrawn.

In the event that any fees are due in connection with this paper, please charge our Deposit Account No. 01-2300.

Respectfully submitted,

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